SYNTHETIC AND BIOLOGICAL STUDIES ON SOME NOVEL OXYGEN, NITROGEN AND SULPHUR CONTAINING HETEROCYCLIC COMPOUNDS

Synopsis

OF THE Ph.D. THESIS TO BE SUBMITTED TO THE

MANGALORE UNIVERSITY

FOR THE AWARD OF THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN

CHEMISTRY

By

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SYNOPSIS OF THE THESIS TO BE SUBMITED TO THE MANGALORE UNIVERSITY

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CHEMISTRY

Title of the Thesis: Synthetic and biological studies on some novel Oxygen, Nitrogen and Sulphur containing heterocyclic compounds

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Name of the Guide **:** Dr. Boja Poojary

Date of Registration **:** 01.03.2017

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Synopsis

Heterocyclic compounds are common structural units in marketed drugs and also in medicinal chemistry targets in the drug discovery process. The main reason behind this is the high prevalence of oxygen, sulfur, and especially nitrogen-containing rings in drug molecules[1]. In the last few decades the chemistry of *N*-bridged heterocycles derived from 1,2,4- triazole and their fused heterocyclic derivatives have received much attention owing to their synthetic and effective medical applications. These *N*-bridged heterocyclic compounds are known to possess significant activity, such as antibacterial[2], anti-inflammatory[3], anticancer[4], anti-allergic[5], antimicrobial[6], antitubercular[7], antiviral[8], antitumor[9], antioxidant[10], anthelmintic[11], anticonvulsant[12,13], antifungal[14], analgesic[15] and antiparasitic[16] properties. Many compounds containing 1,2,4-triazole nucleus are used as drugs; *e.g.,* Loreclezole, Itraconazole and Alprazolam are the triazole-containing anticonvulsant and antifungal drugs and also drugs for panic disorder. Moreover, sulfur substituted 1,2,4-triazole ring systems represents an important group of bioactive compounds[17–20]. In current days non-steroidal drugs Vorozole, Letrozole and Anastrozole are also used for the treatment of cancer. Many drugs containing pyrazoles, like pyrazofurin, phenylbutazone, novalgine, celecoxib, apixaban and ramifenazone are also already in the market. Therefore, 1,2,4-triazole derivatives have the chance in cancer research with good results.

Among the heterocyclic compounds, various pyridine derivatives of commercial interest find applications in market areas mainly due to their important biological activity and their use in agricultural products such as herbicides, insecticides, fungicides and in plant growth regulators.

Pyridine derivatives exhibited various types of biological activities, *viz* antimicrobial[21,22], antibacterial[23], antimycobacterial[24], analgesic[25] antiparkinsonian[26], anticonvulsant[27], antitumoral[28], cytotoxic[29], antimalarial[30], antidiabetic[31], pesticidal[32], inhibitory[33] and receptor antagonists[34].

Similarly, compounds which contain an azomethine group (R-CH=NR_1) is known as Schiff bases, formed by the condensation of a primary amines with carbonyl compounds. Their biological properties are due to the presence of imine group. Therefore it is a good intermediate in the reaction involving the interaction of an enzyme with an amino or a carbonyl group of the substrate. In addition to this, Schiff base are having excellent biological activities such as

antimalarial[35], antibacterial[36], antifungal[37], antiviral[38], antitumor[39] and antioxidant[40] activities. At the same time they have stronger binding affinity towards DNA double helix[41].

In medicinal chemistry, thiophene derivatives have been familiar with their therapeutic applications. There are a variety of reasons why thiophene derivatives are interesting to the pharmaceutical chemists. One is based on the concept of bioisosterism. Thiophene with its six pair of electrons aromaticity and sterically similar to benzene derivatives may well exhibit similar activities. At the same time, the presence of heteroatom in thiophene may alter its metabolic fate, thus thiophene derivatives may have less toxic effects and/or better therapeutic profile[42].

Pyrazoles(1,2-azoles) have proven to be the remarkable scaffolds for the synthesis of biologically active compounds[43-45] due to their wide range of medical applications that center mainly as antimicrobial[46-48], antifungal[44,48,49] anti-inflammatory[50], analgesic and anxiolytic activities[49,51]. Some pyrazole derivatives have also shown antitumor activities towards several cancer cell lines, including leukemia (K562), HeLa cervix adenocarcinoma and Fem-x melanoma[52]. Consequently, in recent years pyrazole-base compounds have become a target of great interest. The various biological and pharmaceutical properties possessed by this important structural motif have attracted the researchers for the development of new drug molecules.

It is well established that compounds that contain sulfur and nitrogen atoms play a significant role in living organisms[53,54]. In particular, thiazolidinone is a well-known heterocyclic compound that contains sulfur and nitrogen atoms. Thiazolidinone moiety can be found in numerous biologically active compounds of natural origin. This is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities such as antimycobacterial[55], antimicrobial[56,57], anticancer[58,59], anticonvulsant[60,61], anti-inflammatory, analgesic[62,63], antiparasitic[64,65], antiviral, anti-HIV[65], antidiabetic[67], antihypertensive[68], antihyperlipidemic[69] and MAO inhibition[70]. The substituted thiazolidinone moiety has attracted considerable interest in the development of biologically active compounds.

Likewise pyrimidine ring is the most basic unit in building DNA and RNA and is found in vitamins like thiamine, riboflavin and folic acid which explains the fact that they possess diverse pharmacological activities including antibacterial[71], antimicrobial[72,73], anti-inflammatory[74], analgesics[75], anticancer[76], antimalarial[77], antitumor[50] and ulcerogenicity[78].

Owing to the immense applications of the aforementioned heterocyclic derivatives in the biological systems along with their advantage of being biocompatible, it was envisioned to synthesize some fused heterocyclic derivatives and investigate their biological properties. Thus the present study aims both at developing the synthetic procedures to access some fused heterocyclic derivatives and investigate their biological applications.

The thesis entitled "**SYNTHETIC AND BIOLOGICAL STUDIES ON SOME NOVEL OXYGEN, NITROGEN AND SULPHUR CONTAINING HETEROCYCLIC COMPOUNDS**" has been divided into the following six chapters.

Chapter 1: A brief review on chemistry of some oxygen, nitrogen and sulphur containing heterocyclic compounds

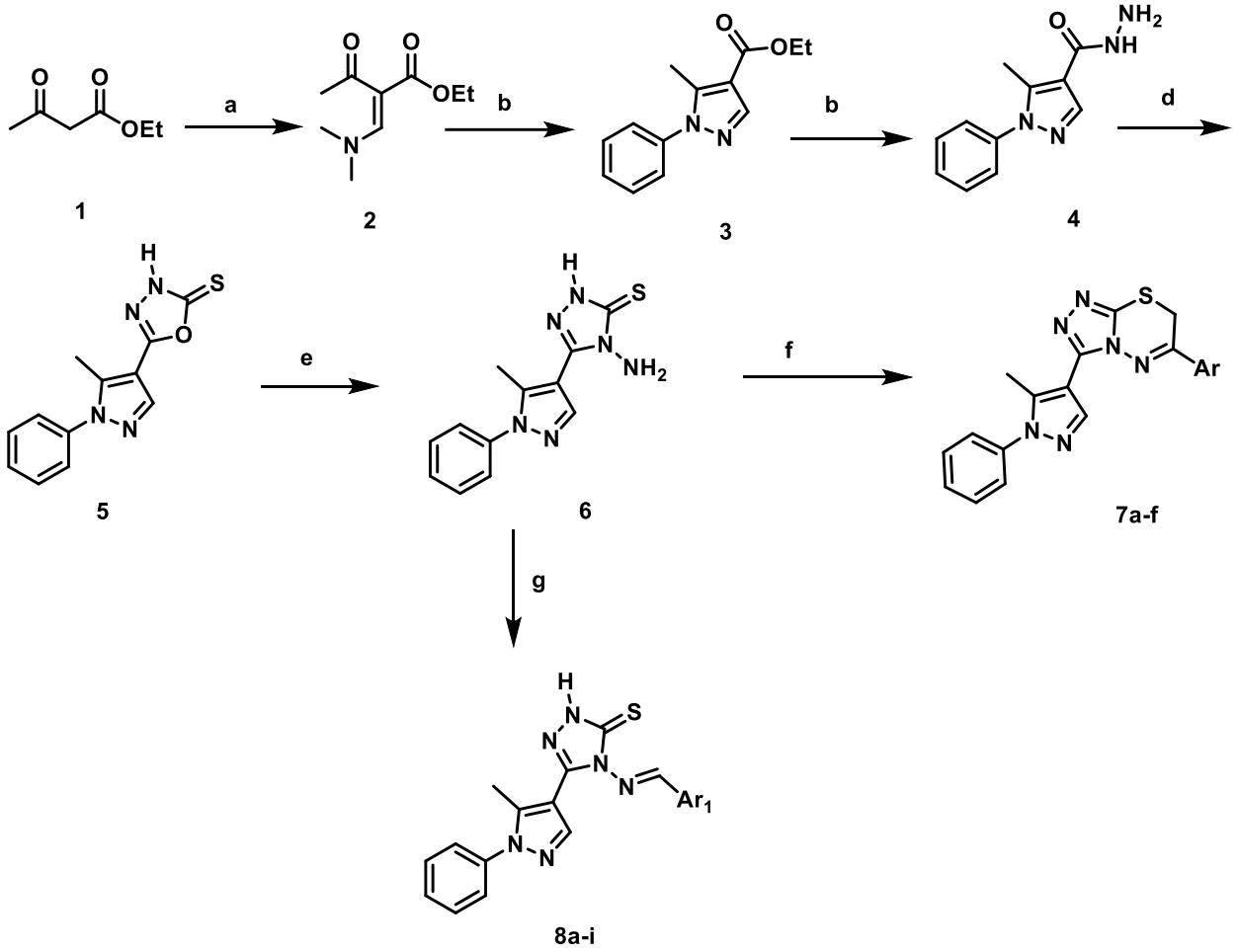
This is an introductory chapter, which deals with a brief account of synthesis and applications of some five and six membered simple and fused heterocyclic derivatives from the publications on chemical literature up to December 2021.

Chapter 2: Synthetic and antibacterial evaluation studies on 1,2,4-triazoles and triazolothiadiazines containing pyrazolyl moiety

This chapter describes the synthesis and characterization of some bioactive thiadiazines and Schiff bases followed by their biological evaluation as antibacterial agents. The synthetic strategy for the synthesis of the target compounds **(7a–f)** and **(8a–i)** is depicted in **Scheme 1**. Following the literature procedure, 5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-1,3,4-oxadiazole-2(3*H*)-thione **(5)**[79,80] was synthesized. Further, the intermediate **(5)** was treated with hydrazine hydrate and refluxed in ethanol to get 4-amino-5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **(6)**. The resultant product was further refluxed with substituted phenacyl bromides in ethanol to obtain 6-aryl-3-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiathiadiazines **(7a–f)**. The intermediate **(6)** was also refluxed with substituted benzylaldehydes in absolute ethanol in presence of catalytic amount of acetic acid to obtain the series of 4-[(arylmethylidene)amino]-5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thiones **(8a–i)**.

All compounds were characterized by elemental analyses, FTIR, ^{1}H NMR, ^{13}C NMR and mass spectroscopic techniques. These compounds were screened for their *in vitro* antibacterial activity by broth dilution method against four bacterial strains. They were also subjected to *in silico*

molecular docking analysis to investigate the significant binding interactions of the target molecules with the binding pockets of prostaglandin D2 synthase [PDB ID: 2VCW], which is the principal requirement for producing the biological effect.



Where, Ar = C_6H_5, 4-F–C_6H_4, 4-Cl–C_6H_4, 4-Br–C_6H_4, 4-Me–C_6H_4, 4-MeO–C_6H_4

Ar_1 = 4-F-C_6H_4, 4-OH-C_6H_4, 2,4-Cl_2-C_6H_3, 2,3-Cl_2-C_6H_3, 3,4-$(OH)_2$-C_6H_3, 3,4-$(OMe)_2$-C_6H_3, 5-Br-2-OH-C_6H_3, 3,4,5-$(OMe)_3$-C_6H_2, 3-Br-4-OH-5-MeO-C_6H_2

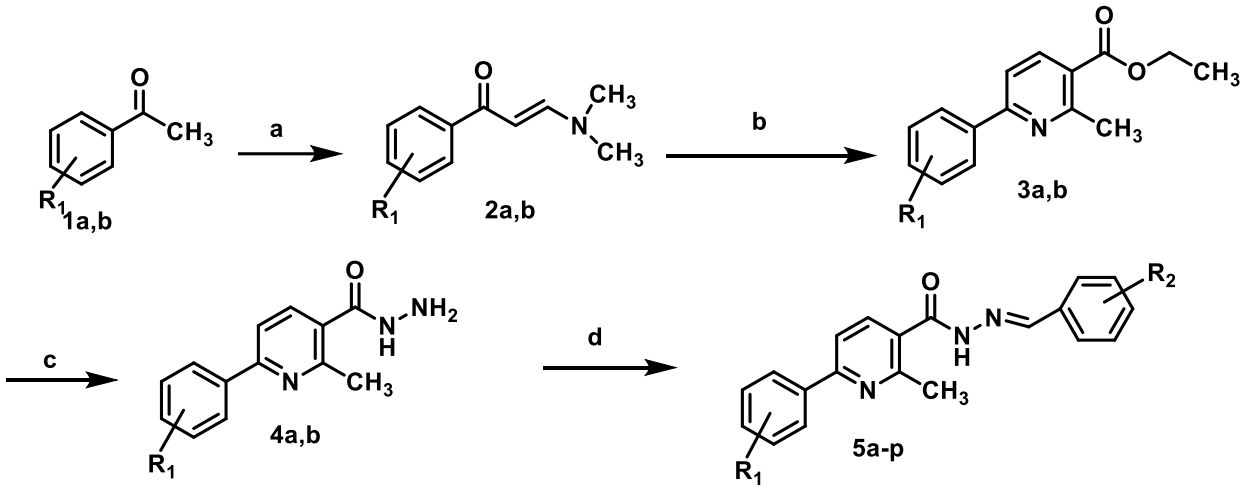
Scheme 1: Synthetic strategy for the thiadiazines and Schiff bases

Reagents and conditions: a) DMF-DMA, 90 ^{0}C, 5-6 h; **b**) Phenyl hydrazine, ethanol, reflux, 3 h; **c**) N_2H_4, reflux, 5-6 h; **d**) CS_2, KOH, EtOH, reflux, 4 h; **e**) N_2H_4, reflux, 5-6 h; **f**) Phenacyl bromide, ethanol, reflux, 5 h; **g**) Aryl aldehyde, AcOH, ethanol, reflux, 6 h.

Chapter 3: Synthesis of novel Schiff bases containing arylpyridines as promising antibacterial agents

This chapter describes the synthesis and characterization of some Schiff bases containing arylpyridines, followed by their biological evaluation as antibacterial agents. The synthetic strategy used for Schiff bases containing arylpyrimidines **(5a-p)** is depicted in **Scheme 2.** The starting material enaminones **(2a,b)** were synthesized in good yield from commercially available 3,4-dichloroacetophenone and 3,4-dimethoxyacetophenone **(1a,b)** by refluxing with *N*,*N*-dimethylformamide dimethyl acetal. The resulting products were subsequently converted into ethyl-6-(3,4-dichloro/3,4-dimethoxyphenyl)-2-methylpyridine-3-carboxylates **(3a,b)** by treating with ethyl acetoacetate in presence of ammonium acetate in glacial acetic acid. Then, the reactions of these intermediates with hydrazine hydrate in absolute alcohol under reflux condition led to the formation of 6-(3,4-dichloro/3,4-dimethoxyphenyl)-2-methylpyridine-3-carbohydrazides **(4a,b)** in good yield. The resultant **4a,b** were further converted into corresponding Schiff bases **(5a-p)** in good yields by condensing them with different substituted benzaldehydes in alcohol by adding the catalytical amount of glacial acetic acid under reflux condition.

All compounds were characterized by elemental analyses, FTIR, ^{1}H NMR, ^{13}C NMR and mass spectroscopic techniques. All synthesized compounds were screened for their *in vitro* antibacterial activity by broth dilution method against four bacterial strains.



Where, R_1 = 3,4-Cl_2, 3,4-$(OMe)_2$

R_2 = 4-F, 4-Me, 4-OH, 2,4-Cl_2, 3,4-$(OH)_2$, 3,4-$(OCH_3)_2$, 3,4,5-$(OCH_3)_3$, 3-Br-4-OH-5-OCH_3

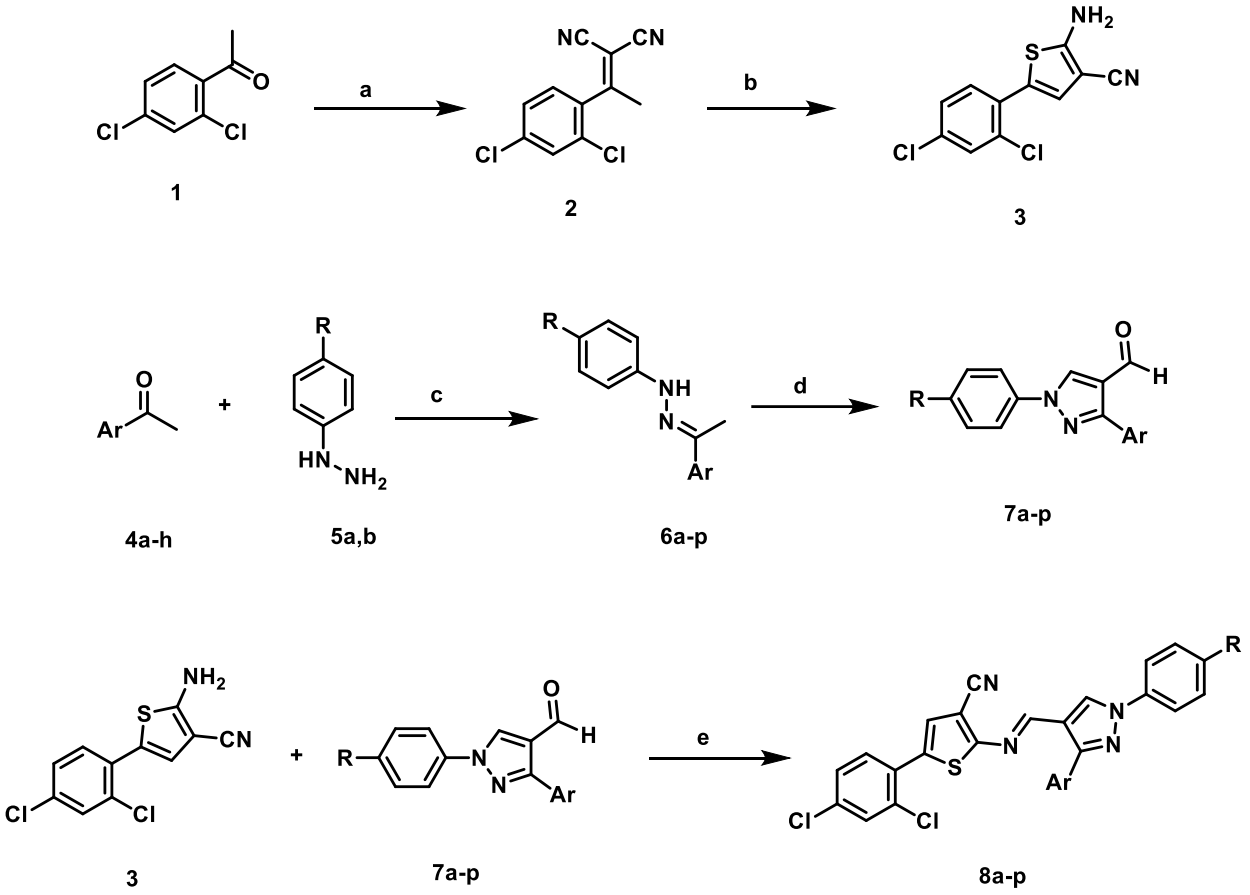
Scheme 2: Synthetic strategy for the Schiff bases containing arylpyridines

Reagents and conditions: a) DMF-DMA, 90 ^{0}C, 5-6 h; **b**) Ethyl acetoacetate, NH_4OAc, AcOH, reflux, 3 h; **c**) N_2H_4, reflux, 5-6 h; **d**) Substituted aromatic aldehydes, AcOH, ethanol, reflux, 5 h.

Chapter 4: Synthesis and pharmacological activities of novel pyrazole clubbed thiophene derivatives

This chapter describes the synthesis and characterization of some pyrazole clubbed thiophene derivatives, followed by their biological evaluation as antibacterial and anti-inflammatory agents. The strategy for the synthesis of pyrazole clubbed thiophene derivatives *via* Gewald synthesis is depicted in **Scheme 3**. Commercially available 2,4-dichloroacetophenone **(1)** upon reaction with malononitrile and ammonium acetate with catalytic amount of acetic acid in toluene under reflux condition afforded 2-(1-(2,4-dichlorophenyl)ethylidene)malononitrile **(2)**. Then it was converted into 2-amino-5-(2,4-dichlorophenyl)thiophene-3-carbonitrile **(3)** by treating with sulfur powder and sodium bicarbonate in THF. 1,3-Disubstituted-1*H*-pyrazole-4-carbaldehydes **(7a-p)** were synthesized by Vilsmeier-Haack reaction in good yields[81]. Finally, preparation of 2-[{(1,3-diaryl-1*H*-pyrazol-4-yl)methylene}amino]-5-(2,4-dichlorophenyl) thiophene-3-carbonitriles **(8a-p)** was achieved by treating the intermediate 2-amino-5-(2,4-dichlorophenyl)thiophene-3-carbonitrile **3** with 1,3-diaryl-1*H*-pyrazole-4-carbaldehydes **(7a-p)** in presence of catalytic amount glacial acetic acid in ethanol with good yield.

All the compounds were characterized by elemental analyses, FTIR, ^{1}H NMR, ^{13}C NMR and mass spectroscopic techniques. These compounds were screened for their *in vitro* antibacterial, anti-inflammatory and anti-tubercular activity. Also, all compounds were tested for their preliminary cytotoxicity by hemolytic assay.



Where, R = 4-H, 4-Cl; Ar = 4-C_6H_5, 4-F-C_6H_4, 4-Cl-C_6H_4, 3-Br-C_6H_4, 4-Br-C_6H_4, 4-CH_3-C_6H_4, 4-OCH_3-C_6H_4, 3-thienyl

Scheme 3: Synthetic strategy for the pyrazole clubbed thiophene derivatives

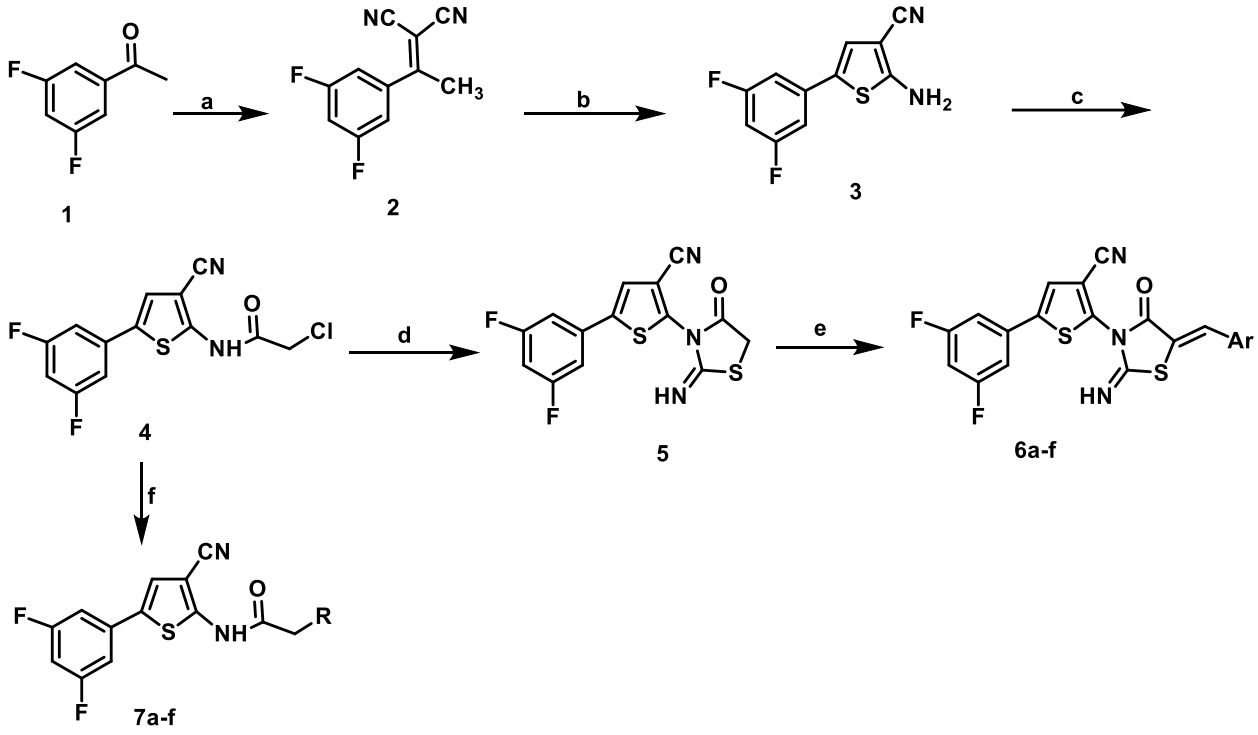
Reagents and conditions: a) Malononitrile, ammonium acetate, acetic acid, toluene, reflux, 24-28 h; **b**) THF, sulfur powder, sodium bicarbonate, water, rt, 24 h; **c**) AcOH, MeOH, reflux, 4 h; **d**) DMF/$POCl_3$, 0-5 ^{0}C, rt, 2 h; **e**) Ethanol, acetic acid (cat.), reflux, 5-7 h.

Chapter 5: Synthesis and biological evaluation of novel thiazolidin-4-one clubbed thiophene derivatives

This chapter describes the synthesis and characterization of some thiazolidin-4-one clubbed thiophene derivatives, followed by the evaluation of their antitubercular and anti-inflammatory activity. The strategy for the synthesis of pyrazole clubbed thiophene derivatives *via* Gewald synthesis is depicted in **Scheme 4**. Initially, 1-(3,5-Difluorophenyl)ethan-1-one **(1)** was converted into 2-(1-(3,5-difluorophenyl)ethylidene)malononitrile **(2)** by treating it with

malononitrile, ammonium acetate and acetic acid. Intermediate, **2** was then treated with sulfur powder in the presence of sodium bicarbonate to yield 2-amino-5-(3,5-difluorophenyl)thiophene-3-carbonitrile **(3)**. A mixture containing 2-amino-5-(3,5-difluorophenyl)thiophene-3-carbonitrile **(3)**, chloroacetyl chloride and K_2CO_3 in chloroform was refluxed to obtain 2-chloro-*N*-(3-cyano-5-(3,5-difluorophenyl)thiophen-2-yl)acetamide **(4)**. In the next step, 5-(3,5-difluorophenyl)-2-(2-imino-4-oxothiazolidin-3-yl)thiophene-3-carbonitrile **(5)** was synthesized by intra-molecular cyclization of compound **4** with potassium thiocyanate in dry acetone. Intermediate **5** was further treated with various aromatic aldehydes and sodium acetate in acetic acid to afford the novel target compounds, **6a-f**. On the other hand, 2-chloro-*N*-(3-cyano-5-(3,5-difluorophenyl)thiophen-2-yl)acetamide **(4)** was refluxed with different aliphatic primary and secondary amines and TEA in 1,4-dioxane to obtain substituted *N*-(3-cyano-5-(3,5-difluorophenyl)thiophen-2-yl)-acetamides **(7a-f)**.

All compounds were characterized by elemental analyses and spectral data. These compounds were screened for their *in vitro* anti-inflammatory and anti-tubercular activity. Also all compounds were tested for their preliminary cytotoxicity by hemolytic assay.



Where, Ar = 4-chlorophenyl, 4-methoxyphenyl, 2,4-dichlorophenyl, 7-methoxy-naphthyl, 1,1'-biphenyl-4-yl, 2-indolyl;
R = propylamino, isobutylamino, diallylamino, piperidino, morpholino, methylpiperazino.

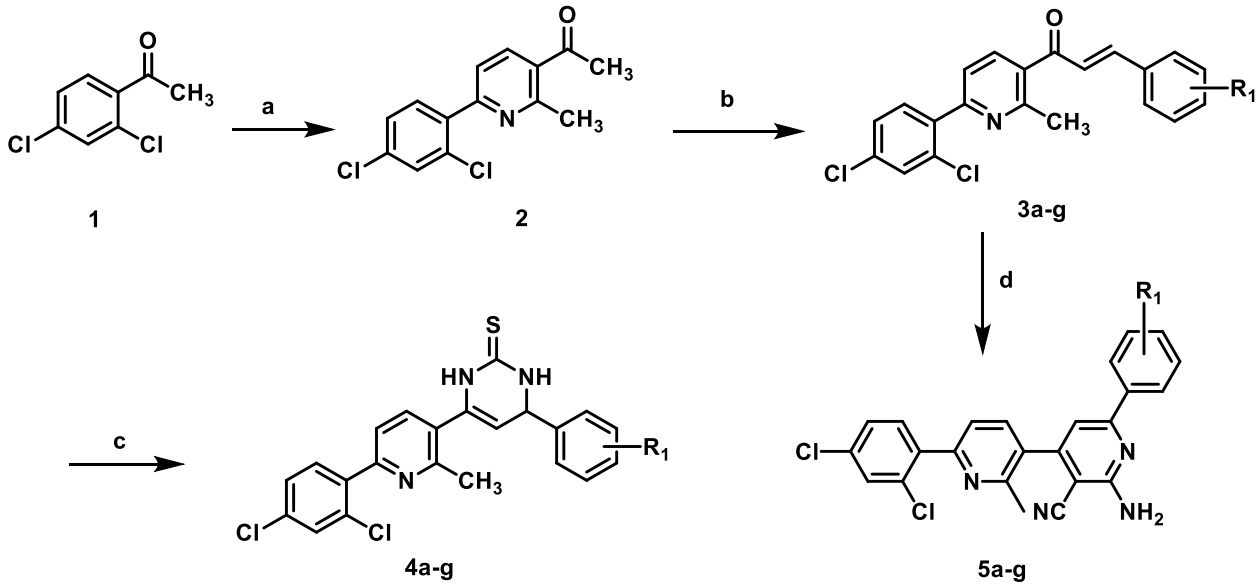
Scheme 4: Synthetic strategy for the thiazolidin-4-one clubbed thiophene derivatives

Reagents and conditions: a) Malononitrile, ammonium acetate, acetic acid, toluene, reflux, 24-28 h; **b**) THF, sulfur powder, sodium bicarbonate, water, rt, 24 h; **c**) chloroacetyl chloride, anhydrous K_2CO_3, reflux, 12 h; **d**) KSCN, dry acetone, reflux, 3 h; **e**) Aromatic aldehyde, NaOAc, AcOH (cat.), ethanol, reflux, 5 h; **f**) Amines, TEA, 1,4-dioxane, reflux, 24 h.

Chapter 6: Synthesis and evaluation of antibacterial and anti-inflammatory activities of novel pyrimidine and 3,4'-bipyridine derivatives

This chapter describes the synthesis and characterization of novel dihydropyrimidine-2(1*H*)-thione and [3,4'-bipyridine]-3'-carbonitrile derivatives, followed by their biological evaluation as antimicrobial and anti-inflammatory agents. The strategy for the synthesis of dihydropyrimidine-2(1*H*)-thiones and [3,4'-bipyridine]-3'-carbonitriles is depicted in **Scheme 5**. Initially, 1-(6-(2,4-dichlorophenyl)-2-methylpyridin-3-yl)-3-aryl-prop-2-en-1-ones (**3a-g**) were synthesized according to the reported procedure[82]. The commercially available 2,4-dichloroacetophenone **1** was refluxed with *N*,*N*-dimethylformamide dimethyl acetal under solvent-free condition to furnish enaminone, **2**. Further, enaminone **2** on treating with acetyl acetone and ammonium acetate in glacial acetic acid media resulted 1-(6-(2,4-dichlorophenyl)-2-methylpyridine-3-yl)ethanone **(2)**. The intermediate 1-(6-(2,4-dichlorophenyl)-2-methylpyridin-3-yl)-3-aryl-prop-2-en-1-ones **(3a-g)** was synthesized by conventional Claisen-Schmidt condensation reaction of 1-(6-(2,4-dichlorophenyl)-2-methylpyridine-3-yl)ethanone **2** with different substituted benzaldehydes in presence of base. The resulting intermediates, **3a-g** was then refluxed with an equal quantity of thiourea in the presence of ethanolic KOH to yield the compounds **4a-g** in good yield. On the other hand, the key intermediate 1-(6-(2,4-dichlorophenyl)-2-methylpyridin-3-yl)-3-aryl-prop-2-en-1-ones **(3a-g)** was treated with malononitrile in presence of ammonium acetate in ethanol under reflux condition to afford the target products, 2'-amino-6-aryl-6-(2,4-dichlorophenyl)-2-methyl[3,4'-bipyridine]-3'-carbonitriles **(5a-g)**.

All compounds were characterized by elemental analyses and spectroscopic data such as FTIR, ^{1}H NMR, ^{13}C NMR and mass spectra. These compounds were screened for their antimicrobial activity *in vitro* by broth dilution assay and anti-inflammatory activity against denaturation of hen's egg albumin method.



Where, R_1 = 4-F, 4-Cl, , 4-Br, 4-Me, 4-OH, 3,4-$(OH)_2$, 3,4-$(OCH_3)_2$.

Scheme 5: Synthetic strategy for the dihydropyrimidine-2(1*H*)-thione and [3,4'-bipyridine]-3'-carbonitrile derivatives

Reagents and conditions: a) DMF-DMA, 90 ^{0}C, 5-6 h and acetylacetone, NH_4OAc, AcOH, reflux, 6 h; **b**) Substituted benzaldehydes, NaOMe, MeOH, stirring, 12-14 h; **c**) Thiourea, KOH, EtOH, reflux, 6 h. **d**) Malononitrile, NH_4OAc, EtOH, reflux 4 h.

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List of Publications

A. Journal Publications

1. Soukhyarani Gopal Nayak, Boja Poojary, 4-[(3,4-Dimethoxybenzylidene)amino]-5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione,*Molbank*, **2019**, *2019 (1)*, M1055.

2. **Soukhyarani Gopal Nayak** and Boja Poojary**,** A Review on the Preparation of 1,3,4-Oxadiazoles From the Dehydration of Hydrazines and Study of Their Biological Role, *Chemistry Africa*, **2019**, *2*, 551–571.

3. **Soukhyarani Gopal Nayak** and Boja Poojary, Synthesis of Novel Schiff Bases Containing Arylpyrimidines as Promising Antibacterial agents, *Heliyon*, **2019**, *5(8)*, e02318.

4. Divyaraj Puthran, Boja Poojary, Nikil Purushotham, Nandam Harikrishna, **Soukhyarani Gopal Nayak**, Vinuta Kamat, Synthesis of Novel Schiff Bases Using 2-Amino-5-(3-fluoro-4-methoxyphenyl)thiophene-3-carbonitrile and 1,3-Disubstituted Pyrazole-4-carboxaldehydes Derivatives and Their Antimicrobial Activity, *Heliyon*, **2019**, *5(8)*, e02233.

5. **Soukhyarani Gopal Nayak**, Boja Poojary, Design, Synthesis, *in Silico* Docking Studies, and Antibacterial Activity of Some Thiadiazines and 1,2,4-Triazole-3-Thiones Bearing Pyrazole Moiety, *Russ. J. Bioorg. Chem.*, **2020**, *46***,** 97-106.

6. Divyaraj Puthran, Boja Poojary, **Soukhyarani Gopal Nayak**, Nikil Purushotham, Mohammed Shafeeulla Rasheed, Hemant Hegde, Design, Synthesis, Molecular docking and Biological Evaluation of Novel Selenium Containing LumefantrineAnalogues. *J. Heterocycl. Chem.*, **2020**, *57(3)*, 1319-1329.

7. Divyaraj Puthran, Boja Poojary, **Soukhyarani Gopal Nayak**, Nikil Purushotham, Manjunath Bhat, Hemant Hedge, Novel Schiff Bases–based Thiophenes: Design, Synthesis and Biological Evaluation, *J. Chin. Chem. Soc.*, **2020**, *67(7)*, 1278-1288.

8. **Soukhyarani Gopal Nayak**, Boja Poojary, Divyaraj Puthran, Vinuta Kamat, Novel Pyrazole Clubbed Thiophene Derivatives via Gewald Synthesis as Antibacterial and Anti-inflammatory Agents. *Arch. Der Pharm.*, **2020**, *353(12)*, 2000103.

9. **Soukhyarani Gopal Nayak**, Boja Poojary, Divyaraj Puthran, Vinuta Kamat, Novel Thiazolidin-4-one Clubbed Thiophene Derivatives via Gewald Synthesis as Anti-tubercular and Anti-inflammatory Agents. *J. Chin. Chem. Soc.*, **2021**, *68(6)*, 1116-1127.

10. Soukhyarani Gopal Nayak, Boja Poojary, Novel dihydropyrimidine-2(1*H*)-thione and [3,4'-bipyridine]-3'-carbonitrile derivatives as a potent antibacterial and anti-inflammatory agents. Communicated to Journal of Heterocyclic Chemistry.

B. Conference Presentations

1. Soukhyarani Gopal Nayak and Boja Poojary, Synthesis, characterization of pyridine containing Schiff base derivates and their pharmacological activity, International conference on "Current Concepts on the role of Indian medicine and phytoceuticals in maintenance of health" and 39th Annual Conference of Indian Association of Biomedical Scientists, held at Jnana Kaveri, Chikka Aluvara Kodagu, Karnataka, India during 15th-17th Nov.2018.

2. Soukhyarani Gopal Nayak and Boja Poojary, Synthesis, Characterization and *in Silico* Molecular Docking Study of a new Series of pyrazole linked heterocycles, National conference on "Synthetic, Spectroscopic and Structural Chemistry (SSSC-2019)" held at Govinda Dasa College, Surathkal, Dakshina Kannada, Karnataka, India during 15th-16th Mar.2019.

3. Soukhyarani Gopal Nayak and Boja Poojary, Synthesis, Characterization and *in silico* Molecular Docking Study of a new Series of thiadiazine and 1,2,4-triazole-3-thione, International conference on "Advanced Functional Materials for Energy, Environment and Health Care (AFMEEHC)" held at Vijnana Bhavan, Manasagangothri, Mysuru, Karnataka, India during 18th-20th Mar.2019.

4. Soukhyarani Gopal Nayak and Boja Poojary, Novel dihydropyrimidine-2(1*H*)-thione and [3,4'-bipyridine]-3'-carbonitrile derivatives as a potent antibacterial and anti-inflammatory agents, International conference on "Advances in Chemical and Materials Science (ICCM - 2019)" held at Department of Chemistry, Mangalore University, Mangalagangothri - 574 199 Dakshina Kannada District, Karnataka India during 17th-19th Oct.2019.

5. Soukhyarani Gopal Nayak and Boja Poojary, Novel Thiophene-3-Carbonitrile Schiff Base Derivatives *via* Gewald Reaction and Their Biological Evaluation, International conference on "Life, Chemical and Health Sciences (ICLCHS-2019)" held at Department of Life Sciences, M. S. Ramaiah College of Arts, Science, and Commerce (RCASC), MSR Nagar, MSRIT Bangalore-560054, Karnataka India during 24^{th}-26^{th} Oct. 2019.

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